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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SEHARASEYON, JEGATHEESAN	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 04/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/067,832	ZIMMET ET AL.	
	Examiner	Art Unit	
	Jegatheesan Seharaseyon, Ph.D	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 November 2005 and 26 January 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7-10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/331,930.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2/8/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election with traverse of Group II, claims 7-10 drawn to a polypeptide in response of 11/9/2005 is acknowledged. Applicants have also further elected SEQ ID NO: 14 with traverse in the response filed in 1/26/2006. Applicants traverse on the basis that invention of Group III (method of treatment/prevention) cannot be practiced in the absence of the invention of Group II (protein). Applicants' arguments have been fully considered but are not considered to be persuasive because protein of Group II could be used for the treatment of Group III or generating antibodies. In addition, inventions of Group III are drawn to methods of treating or preventing of diseases and a search directed to the polypeptide will not automatically lead to the identification of the treatment methods using the polypeptide or protein. Therefore, the searches for each of the groups are not coextensive and would be a burden on the Office to search all of the different claims of the groups. Further with respect to Applicants assertion that the Examiner has not explained the search burden, this requirement is made under 1192 O.G.68 Notice (November 19, 1996), as examination of more than one sequence in one application would result in an undue burden on the PTO (see Office Action dated 9/9/05, pg.5). However, the Office will search the polypeptide encoded by SEQ ID NO: 13 along with SEQ ID NO: 14. The requirement is still deemed proper and is therefore made FINAL. Thus, claims 7-10 are pending and examined. However, Applicants are reminded of rejoinder practices under MPEP § 821.04 (see Office Action dated 9/9/05, pgs. 4 and 5).

Priority

2. If applicant desires priority under 35 U.S.C. § 119(e) based upon a previously filed provisional application, specific reference to the earlier filed application must be made in the instant application. This should appear as the first sentence of the specification following the title, preferably as a separate paragraph. The status of all parent applications (whether abandoned) should also be included.

Information Disclosure Statement

3. The IDS submitted 2/8/02 is acknowledged.

Drawings

4. The drawings submitted 6/3/02 are acknowledged. However, the Office is not clear of the purpose of sheets 1, 5 and 8 because the sequences to be placed in these sheets are recited in the following sheets. Furthermore, the figures are objected to because the sequences presented in Figure 1A and 1B are also provided in the sequence listing. "If the specification includes a sequence listing or a table, such a sequence listing or table is not permitted to be reprinted in the drawings". 37 CFR 1.83(a) and 1.58(a). If a sequence listing, as shown in the drawings, has more information than is contained in the specification, the sequence listing could be included in the specification and the drawings (see MPEP 608.02 [R-3]).

Specification

5. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

Claim Objections

6. Claims 8 and 9 are objected to because of the following informalities: The claims recite sequences not elected by the Applicants. Appropriate correction is required.

Claim Rejections - 35 USC § 112, second paragraph

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 7-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7a. Claims 7 and 10 are rejected for reciting "....a sequence encoding a protein or a derivative, homologue, analogue and mimetic thereof...". The terms derivative, homologue, analogue and mimetic are not defined by the claim and the specification. It is unclear which derivative, homologue, analogue and mimetic are encompassed by the claim. It is also unclear how derivative or homologue or analogue or mimetic is produced in hypothalamus. Additionally, these terms encompass molecules, which are not comprised of amino acids, and it is not clear if these terms are limited to proteins or

would encompass chemical compounds. Therefore, the metes and bounds of the claims are unclear. Claims 8-9 are rejected insofar as they are dependent on claim 7.

7b. Claim 9 is indefinite because the claims recites the "....low stringency conditions at 42°C....". This recitation is relative, and the art does not recognize a single set of conditions for hybridization at "....low stringency conditions at 42°C....". Therefore, the metes and bounds of the claim are unclear. Claims 4-6 are rejected insofar as they depend on rejected claim 10.

7c. The phrase "substantially as set forth" in claims 8 and 9 is relative, which renders the claims indefinite. The term "substantially" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Claim 10 is rejected insofar as they depend on rejected claim 9.

Claim Rejections - 35 USC § 112, first paragraph, written description

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8a. Claims 7-10 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. *This is a written description rejection.*

The specification discloses a protein of SEQ ID NO: 14 and the protein encoded by SEQ ID NO: 13. This meets the written description and enablement provisions of 35 USC 112, first paragraph. However, the specification does not disclose the any protein that is encoded by nucleic acid having at least 60% similarity to all or parts of SEQ ID NO: 13 and/or is capable of hybridizing to SEQ ID NO: 13 under low stringency conditions. The specification also does not disclose amino acid sequences having at least 30% similarity to SEQ ID NO: 14 or of a derivative, homologue, analogue or mimetic thereof which are produced in larger amounts in hypothalamus tissue of obese animals compared to lean animals. Since no activity is described, one cannot conceive a mimetic or derivative. In addition, there is no disclosure with respect to what " derivative" would be expressed in the hypothalamus. Specification also does not disclose variations of the protein (SEQ ID NO: 14), thus one cannot envision a homolog or analog. In addition, there is also no disclosure for agonist and antagonist, because no activity is disclosed there is no way to ascertain if a protein is an agonist or an antagonist. Since no structure or activity is disclosed it is unclear what these are. The claims as written, however, encompass peptide sequences which were not originally contemplated and fail to meet the written description provision of 35 USC 112, first paragraph because the written description is not commensurate in scope with the recitation of claims 7-10. Thus, the specification does not provide written support to the genus encompassed by the instant claims.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The

specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (*See Vas-Cath* at page 1116).

With the exception of peptide of SEQ ID NO: 14 and the polypeptide encoded by SEQ ID NO: 13, the skilled artisan cannot envision all the detailed chemical structure of the contemplated peptide sequences encompassed polynucleotides and/or polypeptides, regardless of the complexity or simplicity of the method of isolation.

Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See *Fiers v. Revel,* 25 USPQ2d 1601, 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Ltd.,* 18 USPQ2d 1016. One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483. In *Fiddes v. Baird,* claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class.

Therefore, only peptide of SEQ ID NO: 14 and the polypeptide encoded by SEQ ID NO: 13, but not the full breadth of the claim meets the written description provision of 35 USC 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. As a result, it does not appear that the inventors were in possession of various sequences set forth in claims 7-10.

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.) Applicants are directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 64, No. 244, pages 71427-71440, Tuesday December 21, 1999.

Claim Rejections - 35 USC § 112, first paragraph, enablement

8b. Claims 7-10 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for protein of SEQ ID NO: 14 and the protein encoded by SEQ ID NO: 13 does not reasonably provide enablement for any protein that is encoded by nucleotide having at least 60% similarity to all or parts of SEQ ID NO: 13 and/or is capable of hybridizing to SEQ ID NO: 13 under low stringency conditions. The specification also is not enabling for amino acid sequences having at least 30% similarity to SEQ ID NO: 14 or of a derivative, homologue, analogue or mimetic thereof which are produced in larger amounts in hypothalamus tissue of obese animals compared to lean animals. In addition, the specification is not enabling for agonist and antagonist. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. See *In re Wands,* 858 F.2d at 737, 8 USPQ2d at 1404. The factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: (1) the breadth of the claims; (2) the nature of the invention; (3) the state of the prior art; (4) the level of one of ordinary skill; (5) the level of predictability in the art; (6) the amount of direction provided by the inventor; (7) the

existence of working examples; and (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The instant claims reads on any protein that is encoded by nucleotide having at least 60% similarity to all or parts of SEQ ID NO: 13 and/or is capable of hybridizing to SEQ ID NO: 13 under low stringency conditions. The specification also reads on amino acid sequences having at least that 30% to SEQ ID NO: 14 or of a derivative, homologue, analogue or mimetic thereof which are produced in larger amounts in hypothalamus tissue of obese animals compared to lean animals. In addition, claims read on all protein agonist and antagonist.

Despite knowledge in the art for producing polypeptides that are derivatives, homologues, analogues or mimetics or agonist or antagonist of a given polypeptide, the specification fails to provide any guidance regarding the changes/differences and yet retain the function. Claims 7-10 recite no function at all and no activity is disclosed for the claimed protein. Furthermore, detailed information regarding the structural and functional requirements of the disclosed protein is lacking. The problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. While it is known that many amino acid substitutions are generally possible in any given protein the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct

three-dimensional spatial orientation of binding and active sites. These or other regions may also be critical determinants of antigenicity. These regions can tolerate only relatively conservative substitutions or no substitutions (see Wells, 1990, Biochemistry 29:8509-8517; Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495). However, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions. Since there is no function or activity recited one cannot test the derivatives, homologues, analogues or mimetics or agonist or antagonist of a given polypeptide. Although it is accepted that the amino acid sequence of a polypeptide determines its structural and functional properties, predicting a protein's structure and function from mere sequence data remains an elusive task. Therefore, predicting which derivative, homologue, analogue or mimetic of the said molecule is expressed in larger amounts in hypothalamus tissue of obese animals compared to lean animals, is well outside the realm of routine experimentation. Also determining the agonist and antagonist of the protein expressed in a larger amount in hypothalamus tissue of obese animals compared to lean animals is well outside the realm of routine experimentation. Thus, undue amount of experimentation would be required to identify sequence of nucleotides encoding or complementary to a sequence encoding a protein or a derivative, homologue, analogue

or mimetic thereof wherein said molecule is expressed in larger amounts in hypothalamus tissue of obese animals compared to lean animals.

Applicants have not taught how one of skill in the art would use the full scope of sequences encompassed by the invention of claims 7-10. The specification as filed does not sufficiently teach one of skill in the art how to make and use the full scope of the claimed sequences. The amount of experimentation required to make and/or use the full scope of the claimed sequences would require trial and error experimentation to determine the nucleotide sequences, which are differentially expressed. Given the breadth of claims 7-10, in light of the unpredictability of the art as determined by the lack of working examples and shown by the prior at of record, the level of skill of the artisan, and the lack of guidance provided in the instant specification, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention.

8c. In addition to the enablement rejection above, the claim 7 is further not enabled for the scope of a "which is produced in larger amounts in hypothalamus tissue of obese animals compared to lean animals." This recitation provides for a claim, similar to single means claims in that it recites "which is produced in larger amounts in hypothalamus tissue of obese animals compared to lean animals" but the specification only discloses compounds described by SEQ ID NO: 14. MPEP 2164.08(a) defines a single means claim as a claim which covered every conceivable means for achieving the stated purpose when the specification disclosed at most only those means known to the inventor. This type of claim was held to be non-enabling for the scope of the claim

in *In re Hyatt* , 708 F.2d 712, 218 USPQ 195 (Fed. Cir. 1983) because the specification disclosed at most only those means known to the inventor. When claims depend on a recited property, a fact situation comparable to *Hyatt* is possible, where the claim covers every conceivable structure (means) for achieving the stated property (result) while the specification discloses at most only those known to the inventor. This appears to be the instant case and the claim is not commensurate in scope with the specification. It would appear that almost any amino acid sequence which is over expressed, in the hypothalamus tissue of obese animals compared to lean animals is encompassed by this claim. Therefore, the claims are clearly not commensurate in scope with the instant specification, absent evidence to the contrary. Claims 8-10 are rejected insofar as they are dependent on claim 7.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9a. Claims 7 and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by Wilding et al. (1993).

The instant invention is directed to the isolated protein or a derivative, homologue, analogue or mimetic thereof wherein said molecule is expressed in larger amounts in hypothalamus tissue of obese animals compared to lean animals.

Wilding et al. teaches that the somatostatin peptide is present at a higher concentration in the hypothalamus of obese mouse compared lean mouse (see Table 2). Therefore, the disclosure of Wilding et al. anticipates the inventions of claims 7 and 10.

Conclusion

10. No claims are allowable. However, claims drawn to protein of SEQ IDNO: 14 and the protein encoded by SEQ ID NO: 13 are allowable over prior art.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jegatheesan Seharaseyon, Ph.D whose telephone number is 571-272-0892. The examiner can normally be reached on M-F: 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on 571-272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should

you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JSS 4/4/06

CHRISTINE J. SAOUD
PRIMARY EXAMINER

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